

# Dynamic Hip Screw versus Proximal Femoral Nail in the Management of Intertrochanteric Fractures - A Retrospective Analysis from Rajasthan

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## ABSTRACT

### BACKGROUND

Current management of Intertrochanteric (IT) fractures has evolved with the introduction of dynamic hip screw (DHS) and proximal femoral nail (PFN). The purpose of this study was to compare the functional outcomes between the DHS and PFN for IT fracture fixation.

### METHODS

This study is a retrospective comparative analysis of 455 patients with IT fractures; DHS (292) and PFN (163), who were treated from June 2012 to June 2015. The patients were reviewed postoperatively for a minimum of 12 months to evaluate functional outcome using Salvati-Wilson score. Categorical data was present as absolute number or percentages, and parametric variables were presented as Mean  $\pm$  SD, while non parametric data were presented as median. Statistical significance was defined as  $P < 0.05$ .

### RESULTS

Intramedullary nails offer no advantage over extramedullary devices to treat IT fractures caused by low-energy trauma (AO 31 - A1). However, clinically significant outcomes were established for PFN group in terms of duration of surgery, x-ray exposure and SW Score for AO / OTA 31 - A2 and 31 - A3. Reoperations encountered for local pain due to implant prominence were significantly higher in the PFN group (4.90 % versus 1.02 %). Kaplan Meier survival probability of 69.3 % and 79.5 % predicted for DHS and PFN respectively, 3 years postoperatively.

### CONCLUSIONS

Our conclusion reinforces indication for PFN in unstable IT fractures (31 - A2 and 31 - A3), owing to its better functional outcome and biomechanical properties. Functional outcomes for stable IT fracture (AO 31 - A1) were comparable between DHS and PFN, therefore final decision for implant choice depends on implant cost, surgeon's preference for specific technique. However, understanding the morphology of proximal femur, peritrochanteric region is crucial to analyse the anatomical variations in Indian population which will provide the basis for intramedullary nail design modifications.

### KEYWORDS

Intertrochanteric Fractures, DHS Fixation, PFN Fixation

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## BACKGROUND

Intertrochanteric (IT) fractures are the most frequent injuries in elderly osteoporotic patients; however, high energy trauma in young people can cause similar fracture pattern. These fractures continue to consume a considerable fraction of our health care resources, remain a challenge to date because of osteoporosis and associated multiple comorbidities., despite distinct improvements in surgical technique, implant design, and patient care.<sup>1-4</sup> The frequency of these fractures has increased primarily, sedentary lifestyle brought on by urbanization and increasing life span are prime factors for the increase.

It is estimated that there will be a steep rise in the incidence of hip fracture in the near future. Worldwide cases would double to 2.6 million by 2025 and almost quadruple to 6.26 million by 2050. Asia and Latin America will observe a sharp rise in hip fractures percentage from 37 % in 2025 to 45 % in 2050. About, 90 % of IT fractures in elderly patients result from simple fall. Osteoporosis accounts for a higher incidence of trochanteric fractures in females as compared to male population.<sup>5</sup>

In a study on Swedish population of more than 20,000 patients, women after the age of 30 years had hip fracture incidence doubled every 5.6 years.<sup>6,7</sup> In addition to high mortality rates<sup>1</sup> ranging from 14 % to 47 % and overall cost, almost half of these patients needed assistance in one or more activities of routine life. To address and organize the health care burden, multidisciplinary integrated team approach is becoming increasingly common.

The trochanteric fracture management by non operative methods was quite prevalent before the introduction of internal fixation devices. This approach was associated with complications of varus collapse leading to malunion, external rotation deformity, shortening, limitation of hip movements and prolonged immobilization like deep vein thrombosis, bedsores and respiratory infections.<sup>8</sup> Being aware of all these factors, early surgical intervention with anatomical reduction and stable internal fixation is utmost important to improve patient outcomes. Various forms of internal fixation devices are available for trochanteric fractures. Dynamic Hip Screw (DHS) with side plate assemblies is used most frequently<sup>9-10</sup> and is the mainstay of fixation that permits a controlled collapse of proximal fracture fragment on the fixation device while maintaining stability and thus encouraging fracture union. Fractures with posteromedial comminution, lateral wall collapse, subtrochanteric extension or reverse oblique pattern are inherently deficient of fracture stability known as unstable are difficult to manage with DHS alone.

Several studies have emphasized the significance of intramedullary nail as a treatment of choice particularly for unstable fracture because of its stable biomechanical construct and lower failure rates.<sup>11,12</sup> still, other series have reported good outcomes with favourable reoperation rates for dynamic hip screw.<sup>13,14</sup> The scientific evidence supporting either treatment is limited and to some extent conflicting. Therefore, a definitive consensus has not been reached.<sup>15-18</sup>

## Objectives

### Primary Objective

To compare the functional outcomes between the DHS and PFN for IT fracture fixation using Salvati and Wilson scoring (SWS) system

### Secondary Objectives

1. Radiological assessment for fracture healing, shortening, Non-union, failed osteosynthesis, Screw cut out, Z phenomenon, implant prominence, Refracture.
2. Comparison of intraoperative variables including duration of surgery, ease of procedure, fluoroscopic exposure.
3. Duration of hospital stay.
4. Postoperative complications.

## METHODS

This retrospective comparative analysis consisted of patients of all age groups who were treated for acute IT fractures. For this study, data on 546 patients were collected from January 2012 to December 2015 at the Department of Orthopaedics, Medical College, Kota, Rajasthan. The study protocol and consent forms were approved by the institutional review board. A detailed informed consent form was signed by each patient and all the information was kept confidential. Fractures operated with implants other than DHS or a nail (N = 22), pathological fractures (N = 12) and deceased or follow up dropouts (N = 57) were excluded from the study. The remaining fractures treated with a DHS (N = 292) or PFN (N = 163) were taken for final analysis.

### Inclusion Criteria

1. Patients with isolated IT fractures operated either with DHS or PFN
2. Ambulatory independently prior to fracture

### Exclusion Criteria

1. Pathological IT fracture
2. Fracture operated with implants other than PFN or DHS
3. Associated femoral neck fracture or polytrauma patients
4. Follow up drop out or Deceased patients.

The radiographs of pelvis with both hip anterior posterior (AP) with both limb parallel, neutral rotation and lateral view of fracture hip with proximal femur were taken. Peritrochanteric fractures which constituted of Intertrochanteric and subtrochanteric fractures were classified according to orthopaedic trauma association (OTA) and AO classification.<sup>19</sup> After adequate preoperative planning and pre-anaesthetic check up, surgical clearance with operative risk as per American society of anaesthesiologist (ASA) grading (ASA 1 Normal healthy patient to ASA 5 moribund patient), patients were operated under combined spinal epidural anaesthesia (CSEA) using either DHS with standard lateral approach or PFN with supratrochanteric entry point incision as fixation device

under fluoroscopic guidance. Intraoperative variables including surgical duration, fluoroscopic exposure, blood loss and ease of surgical procedures were documented. Patients were made to exercise and to learn postoperative rehabilitation protocol under guidance of experts. Radiographs were taken 48 hours after surgery to assess fracture characteristics like adequacy of reduction, alignment in coronal and sagittal plane and implant position, screw length etc. The data on functional recovery were obtained using Salvati and Wilson scoring (SWS) system which included hip pain, ability to walk with or without support, muscle power, hip joint motion and function.<sup>20</sup> SWS grading is as following with maximum score value of 40 (score > 31 excellent, 24 - 30 good, 16 - 23 fair and < 16 poor). Any type of redo surgery during follow-up was considered a reoperation. Reoperations were categorized according to reason for reoperation and type of reoperation performed.

**Follow Up**

The patients were reviewed postoperatively for a minimum of 12 months for evaluation of clinical, functional outcome using SWS score and radiological assessment for fracture healing and other complications like deformity, implant prominence, failed osteosynthesis, Z effect, screw cut out, peri implant refracture at 6 weeks, 3 months, 6 months and yearly thereafter. The mean follow up was 31.90 months (range 12 to 53 months) for the DHS group and 23.31 months (range 13 to 40 months) for the PFN group.

**Statistical Method**

The statistical analysis was conducted using the statistical package for social science (SPSS Inc. released 2009, Version 18.0.) For sample size calculation, we hypothesized that the functional outcomes offered by PFN would be 10 % better than DHS with a SD of 20 %, according to previous studies.<sup>24</sup> The minimum sample size calculated by comparing two means was 141 patients per group for a power of 80 % with a 2 - tailed significance level of 5 % ( $\beta = 0.2$  &  $\alpha = 0.05$ ). In our study 455 patients; DHS (292) and PFN (193) were taken respectively to reduce the risk of  $\beta$  error that happened in previous studies because of small sample size.<sup>16,36,37</sup> Categorical data was present as absolute number or percentages and parametric variables were presented as Mean  $\pm$  SD, while non parametric data were presented as median (95 % Conf. Interval). Normality of data was assessed by using Shapiro - Wilk test along with skewness and kurtosis. In the Kaplan Meier survival analysis, to calculate survival time, reoperation of any kind was considered the endpoint. Survival time for patients without reoperations was censored at the end of study as dropout / migration or death. All patients were included in the Kaplan-Meier analysis applied to determine the proportion of reoperations after final follow up. Statistical analysis for parametric variables was done using unpaired Student 't' test. Differences between groups were assessed with Chi-square or Fisher's exact test for categorical variables. Statistical significance was defined as  $P < 0.05$ .

**RESULTS**

Baseline characteristic including age, sex, side, and mode of injury, ASA grade and mean hospital stay were comparable in between DHS and PFN groups. However, a large proportion of unstable fractures (AO 31 - A2, A3) were in the PFN group. (Table 1) Mode of injury was fall at home or outdoors in majority of patients (90.06 % and 87.11 %) in DHS and PFN respectively. Women were more prone to peritrochanteric fracture as compared to men (56 % and 59 % versus 44 % and 42 % for DHS and PFN group respectively).

Variables		DHS Group (N = 292)	PFN Group (N = 163)	P Value
<b>Mean Age (Years)</b>		<b>68.21 <math>\pm</math> 14.16</b>	<b>69.28 <math>\pm</math> 12.36</b>	<b>0.401</b>
Sex	Male (%)	128 (43.83)	66 (41.71)	0.55
	Female (%)	164 (56.16)	97 (59.50)	
ASA grade	1 (%)	30 (10.20 %)	21 (12.88)	0.489
	2 (%)	99 (33.90 %)	48 (29.44)	0.384
	3 (%)	147 (46.59 %)	84 (51.53)	0.884
	4 (%)	16 (5.44 %)	10 (6.13)	0.834
	5 (%)	0	0	00
Mode of injury	Fall at home/outdoor	263 (90.06 %)	142 (87.11 %)	0.418
	Road traffic accident	29 (9.93 %)	23 (14.11 %)	0.234
AO/OTA classification	A1	122 (41.78 %)	58 (35.58 %)	0.231
	A2	131 (44.86 %)	61 (37.42 %)	0.149
	A3	39 (13.35 %)	44 (26.99 %)	0.0005
	Deceased	43 (14.72 %)	14 (8.58 %)	0.08
Mean F / U duration (months)		31.90 $\pm$ 10.93	23.31 $\pm$ 8.75	< 0.0001

**Table 1. Comparison of Baseline Characteristics**

Variables	DHS Group	PFN Group	P Value
Mean Duration of Sx (Minutes)	49.53 $\pm$ 8.32	39.57 $\pm$ 9.36	< 0.0001
Mean Hospital stay (Days)	8.54 $\pm$ 1.84	8.26 $\pm$ 2.02	0.9793
SW hip score	27.33 $\pm$ 5.77	28.49 $\pm$ 6.37	0.1287

**Table 2. Comparison of Functional Recovery and Surgical Time**

Reoperated Hips	DHS	PFN	P Value	
	<b>48 (16.43 %)</b>	<b>25 (15.33 %)</b>	<b>0.862</b>	
Reoperation cause	Failed osteosynthesis	16 (5.47 %)	4 (2.45 %)	0.203
	Non-union	3 (1.02 %)	1 (0.06 %)	0.650
	Z effect	4 (1.36 %)	5 (3.06 %)	0.370
	Screw Cut out	11 (3.76 %)	3 (1.84 %)	0.650
	Peri Implant Refracture	5 (1.71 %)	2 (1.22 %)	0.819
	Infection	6 (2.05 %)	2 (1.22 %)	0.717
	Local Pain due to Implant prominence	3 (1.02 %)	8 (4.90 %)	0.02
Reoperation type	New Osteosynthesis	15	9	0.830
	Implant removal	7	11	0.04
	Bipolar hemiarthroplasty	10	5	0.876
	Total hip replacement	14	3	0.128
	Drainage	5	3	0.920

**Table 3. Different Reasons for Reoperation and Types of Reoperations**

The average surgical time for PFN was shorter (39.57 minutes) than DHS (49.53 minutes) ( $P < 0.0001$ ), so was intraoperative x-ray exposure and blood loss. Mean hospital stay was 8.54 days and 8.26 days while Mean SW hip score was 27.33 and 28.49 respectively for DHS and PFN groups (Table 2). So, there was no statistically significant difference in terms of mean hospital stay and functional recovery assessed by using SW hip score. ( $P = 0.9793$ ,  $P = 0.1287$ ). However, patients operated with PFN for AO type 31. A2 and 31. A3 (unstable fracture) fared better than DHS group in

term of mean SW score ( $P = 0.014$ ,  $P = 0.012$ ) (Table 4). Patients in the DHS group exhibited a higher proportion of reoperations as compared to the PFN group ( $P = 0.862$ ) (Table 3). The percentage of reoperations was 16.43 % ( $N = 292$ ) for the DHS group and 15.33 % ( $N = 163$ ) for patients treated with PFN. A detailed description of reasons and types of reoperations performed is shown in Table 3. It was AO type 31. A3 in the DHS group which had the highest reoperation rate (30.76 %) (Table 4).

Reoperations encountered for failed osteosynthesis were more in the DHS group (5.47 % versus 2.451 %,  $p = 0.203$ ) whereas local pain due to implant prominence was

significantly higher in PFN group (4.90 % versus 1.02 %,  $p = 0.02$ ).

However, reoperations encountered for reasons other than mentioned above such as Z effect, non-union, infections, failed osteosynthesis, screw cut-out, or peri-implant fractures were not statistically significant between the DHS and PFN groups.

Kaplan Meier analysis predicted 95.7 % survival probability for DHS and 94.9 % for PFN group at 1 year whereas it was 69.3 % and 79.5 % for DHS and PFN respectively, 3 years postoperatively. (Figure 1)

Variables	31-A1			31-A2			31-A3			
	DHS (N = 122)	PFN (N = 58)	P Value	DHS (N = 131)	PFN (N = 61)	P Value	DHS (N = 39)	PFN (N = 44)	P Value	
Mean Age (Years)	67.95 ± 12.96	71.34 ± 8.30	0.069	67.32 ± 14.78	68.09 ± 11.16	0.717	73.10 ± 14.85	71.56 ± 14.40	0.633	
Sex	Male (%)	54 (44.26 %)	23 (39.65 %)	0.672	56 (42.74 %)	25 (40.98 %)	0.941	18 (46.15 %)	20 (45.45 %)	0.949
	Female (%)	68 (55.73 %)	35 (60.34 %)		75 (57.25 %)	36 (59.01 %)		21 (53.84 %)	24 (54.54 %)	
ASA Grade	1 (%)	11 (9.01 %)	6 (10.34 %)	0.788	14 (10.68 %)	8 (13.11 %)	0.632	5 (12.82 %)	7 (15.90 %)	0.762
	2 (%)	39 (31.96 %)	17 (29.31 %)	0.863	48 (36.64 %)	19 (31.14 %)	0.561	12 (30.76 %)	12 (27.27 %)	0.913
	3 (%)	53 (43.44 %)	32 (55.17 %)	0.153	65 (49.61 %)	29 (47.54 %)	0.910	19 (48.71 %)	23 (52.27 %)	0.917
	4 (%)	5 (4.09 %)	3 (5.17 %)	0.713	7 (5.34 %)	5 (8.19 %)	0.529	4 (10.25 %)	2 (4.54 %)	0.412
	5 (%)	0	0	0.00	0	0	0.00	0	0	0.00
Mode of injury	Fall at home/outdoor	113 (92.62 %)	52 (89.65 %)	0.700	117 (89.31 %)	49 (80.37 %)	0.11	32 (82.05 %)	36 (81.81 %)	0.978
	RTA	9 (7.37 %)	6 (10.34 %)		14 (10.68 %)	12 (19.67 %)		7 (17.94 %)	8 (18.18 %)	
Mean Duration of Surgery (Minutes)	42.54 ± 3.47	30.25 ± 4.12	< 0.0001	52.27 ± 5.60	40.40 ± 5.26	< 0.0001	62.94 ± 5.22	50.68 ± 5.01	< 0.0001	
Mean Hospital Stay (Days)	8.40 ± 1.57	8.48 ± 1.59	0.750	8.44 ± 1.90	7.78 ± 2.00	0.028	9.30 ± 2.22	8.65 ± 2.44	0.210	
SW Hip Score	27.98 ± 5.46	27.37 ± 5.22	0.478	27.53 ± 5.86	29.86 ± 6.53	0.014	24.36 ± 5.56	28.04 ± 7.27	0.012	
Reoperation	Implant prominence	0	2		2	4		1	2	
	Non-union	0	0		1	1		2	0	
	Infection	3	1		2	0		1	1	
	Z effect	1	1		2	2		1	2	
	Cut out	3	0		6	2		2	1	
	Failed osteosynthesis	2	1		9	2		5	1	
	Refraction	2	1		3	0		0	1	
<b>Total</b>	<b>11 (9.01 %)</b>	<b>6 (10.34 %)</b>	<b>0.990</b>	<b>25 (19.08 %)</b>	<b>11 (18.03 %)</b>	<b>0.862</b>	<b>12 (30.76 %)</b>	<b>8 (18.18 %)</b>	<b>0.279</b>	

Table 4. Comparison between Different AO/OTA Fracture Types

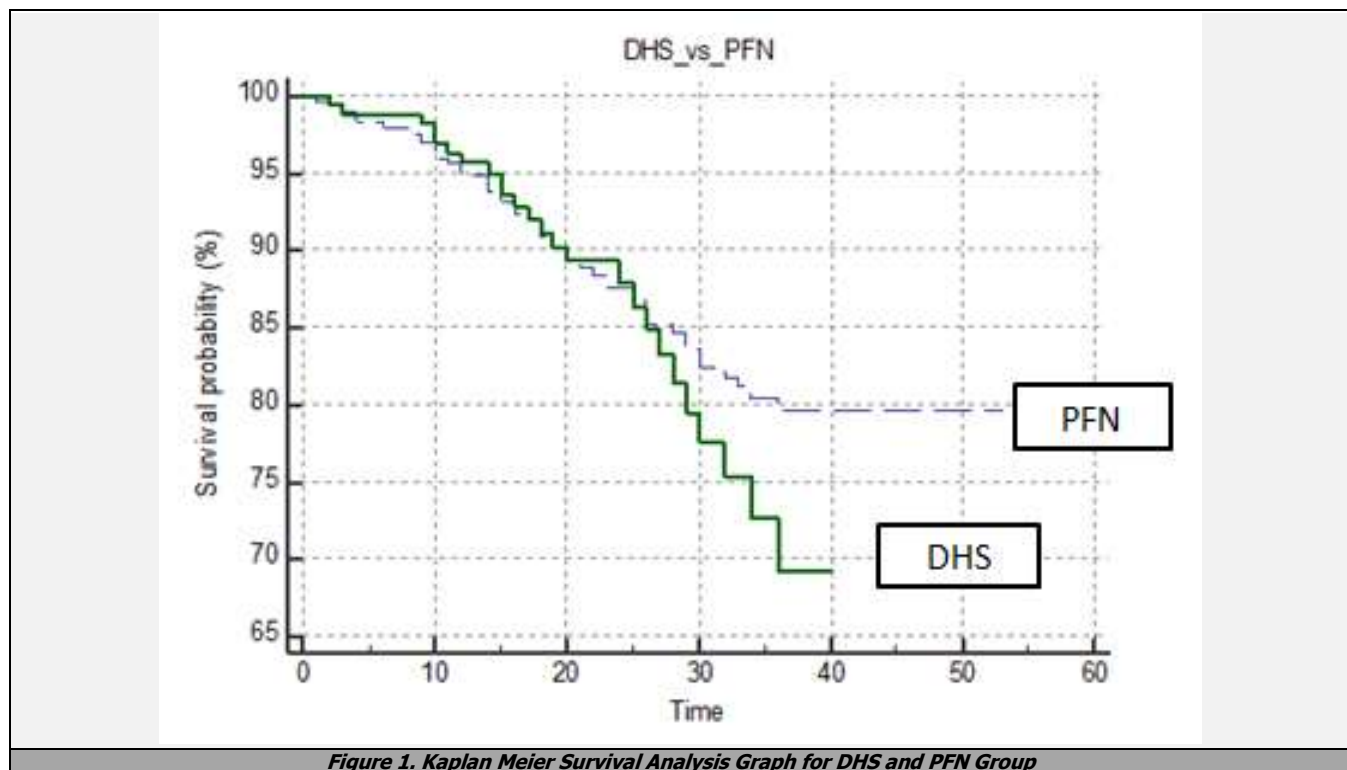


Figure 1. Kaplan Meier Survival Analysis Graph for DHS and PFN Group

## DISCUSSION

In the present study, comparing DHS and PFN for IT fractures, we found more reoperations for patients operated with a DHS. In addition, results regarding functional outcomes (SWS score) were all slightly in favour of PFN particularly in type AO / OTA 31 - A2 and 31 - A3 fractures. Treatment of unstable (reverse oblique, subtrochanteric extension, posteromedial comminution) fractures with a DHS is not considered appropriate by some studies, in particular due to biomechanical considerations.<sup>12,21</sup> However, the evidence in the literature is not obvious and conflicting, whether to use IM nail or DHS in these fractures.<sup>15-18</sup>

Patient population in this study had a particularly high female-to-male ratio (6: 4), as reported elsewhere.<sup>1</sup> Mode of injury in overall 90 % patients was due to trivial trauma (fall from standing height). These results are consistent with previous studies that have also suggested the high prevalence of low energy trauma, mainly falls at home.<sup>16,22</sup> In 2013, study in Norway registry of 1792 SHS and 92 IM nail devices for reverse oblique and subtrochanteric fractures showed no clinically significant difference in EurQol 5 dimensions questionnaire, pain or satisfaction. However, SHS group had higher reoperation rate.<sup>2</sup> Present study also have reoperation rates of 16.43 % and 15.33 % at final follow up for DHS and PFN respectively and are comparable to most other studies on unstable pertrochanteric fractures.<sup>13,23-26</sup> Still, significantly higher failure rates for the DHS group have been reported in particular for AO / OTA 31 - A3 type (30.76 %).<sup>11,27,28</sup>

Brammer and colleagues in their study included 101 reverse oblique trochanteric fractures and found a considerably lower fracture healing rate of 9 %, though no statistically significant difference in reoperation rate between IM nails and DHS was established.<sup>14</sup> Some other studies also have shown more favourable complication rates for the DHS treated patient.<sup>13,29</sup> Few randomized clinical trials have compared extra-medullary implants other than DHS in subtrochanteric fractures (frequently including AO / OTA type A3 trochanteric fractures). Ekstrom et al.<sup>30</sup> reported that reoperation rate in IM nailing group was significantly higher (9 % vs. 1 % reoperations), whereas results by Miedel et al. showed higher reoperation rate for Medoff sliding plate group compared to nailing group (3 out of 12 compared to 0 out of 16 in the nailing group) which was not clinically significant.<sup>26</sup> However, IM nail group have lower reoperation rates compared to DCS / blade plate group as published by Sadowski et al. and Rahme et al. in their respective studies.<sup>27,31</sup>

No standardized criteria for assessment of functional outcomes has been used in various comparative trials reported in the existing literature for pertrochanteric fractures. Taken together, no major or consistent difference in such outcome parameters has been established and our findings are also in accordance with the data published,<sup>9,28</sup> Lesser pain in the PFN treated patients can be contributed to stable intramedullary fixation construct and / or mini invasive surgery in the early postoperative period, whereas

long term differences might be as a result of more local pain from protruding hardware impinging abductor mechanism in the PFN group. The cause for most reoperations (N = 8) in the PFN group was painful prominent nail at greater tuberosity (GT) which was hindering cross leg sitting, side turning on the operated side. Apart from these cases most patients, particularly females had PFN protruding out GT clinically as well as radiologically. So there is a need for development of better implant design which can accommodate greater trochanter height for Indian population. Along with this, two cases (versus 5 in DHS group) of peri implant femur fracture occurred in patients operated with PFN and are consistent with Bhandari et al.<sup>32</sup> findings, where the rate of femoral fractures was low and comparable to DHS that might represent an under-reporting or could be due to improvements in implant design and surgical technique.

The PFN demonstrates more value for load to failure and thus tolerates greater static as well as cyclic loading than the DHS. Secondly, it provides efficient load transfer therefore fracture consolidates with PFN even in the absence of medial support. Because of its intramedullary position PFN compensates for deficient medial column. Thirdly, shorter lever of IM device decreases tensile strain thus reducing failure rate compared to extramedullary devices.<sup>11-12</sup> Other studies have shown that the DHS is technically simple, has advantage of controlled impaction, allows early weight-bearing, associated with low complication rates, hence considered reliable method for IT fracture stabilization.<sup>9-10,13,29</sup>

Several studies have demonstrated differences in treatment outcome, as in the present study while comparing the DHS with IM Nail device<sup>24,33,34</sup> but Saudan et al.<sup>16</sup> found no difference in social functioning and mobility scores between the DHS and PFN groups in terms of return to pre-fracture levels of ambulation and independence, at 1-year follow-up. They concluded that both devices were comparable and did not offer any advantage over the other for the treatment of IT fractures caused by low-energy trauma (AO types 31. A1 and 31. A2). Dujardin et al.<sup>22</sup> showed that IM nail enabled relatively faster hip strength, mobility and functional recovery. This trend was similar in the first 3 months but became significantly apparent 6 months after surgery.

In the current study, assessment of SWS scores were 27.33 and 28.49 for DHS and PFN group respectively (P = 0.1287) like in the Saarenpa et al. study,<sup>24</sup> there were no between-group differences in final scores (P = 0.478). However, patients with AO 31 - A2 and A3 type fractures showed statistically significant SWS scores for the PFN group (27.35 versus 29.86 and 24.36 versus 28.04 respectively) at final follow up (P = 0.014, P = 0.012).

Overall functional scores are similar for stable pertrochanteric fracture, still PFN technique exhibited better functional improvement and Kaplan Meier survival probability at 3 years, unlike DHS-treated patients in particular for unstable IT fractures. In practice, this means that PFN treatment is associated with better longevity in

terms of reoperations and faster improvement in quality of life than the DHS technique.

## CONCLUSIONS

Our conclusion reinforces indication for PFN in unstable IT fractures (31 - A2) and high subtrochanteric fractures (31 - A3), owing to its better functional outcome, shorter operation time, lesser disturbance to vascularity of fragments, early weight bearing, limited open reduction and superior mechanical properties. Functional outcomes for stable IT fracture (AO 31 - A1) were comparable, therefore final decision for implant choice depends on implant cost, surgeon's preference for specific technique. However, concern regarding implant design should be emphasized because pain due to implant prominence (PFN) is still a concern in Indian population. Therefore, understanding the morphology of proximal femur and pertrochanteric region is crucial to analyse the anatomical variations in Indian population which will provide the basis for intramedullary nail design (PFN) modifications.

## Limitations

Our study still has various limitations. Since it is a retrospective comparative analysis instead of randomized control trial (RCT), it might have selection bias. For example, operating surgeon's level of experience, fracture classification by operating surgeon, surgical indications, implant preferences, postoperative rehabilitation protocol might differ and contribute to selection bias. In developing countries like India where implant cost plays a major role in implant selection, choosing one implant over another, even if results are otherwise not equivalent is considered. However, various patient characteristics including age, gender, ASA grade, mode of injury were similar for the two implant groups; a selection bias is less likely. Therefore, our findings should be interpreted with caution.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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